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EXAMINER

KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 08/01/2003

23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n No.

09/500,747

Applicant(s)

GOKHALE ET AL.

Examin r

Kathleen M Kerr

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-- The MAILING DATE of this c mmunicati n appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

- 4) ☒ Claim(s) 23,25,26 and 28-39 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23,25,26 and 28-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Application Status

1. In response to the previous Office action, a Final rejection (Paper No. 19 mailed November 5, 2002), Applicants filed a request for continued examination (Paper No. 21) and an amendment (Paper No. 22) on May 8, 2003. Said amendment amended Claims 26 and 28-39. Claims 23, 25, 26, and 28-39 are pending in the instant application and will be examined herein.

Priority

2. As previously noted, the instant application is granted the benefit of priority for the U.S. Provisional Application No. 60/119,363 filed on February 9, 1999.

Drawings

3. In response to the previous Office action, Applicants filed a complete set of three drawings considered by the Draftsman. The drawings have been approved by the Draftsmen and are entered as formal drawings acceptable for publication upon the identification of allowable subject matter.

New – Objections to the Specification

4. The specification is objected to for not having updated patent application information. On page 5, line 17 and again on page 13, line 11, U.S. patent application 09/346,860 is referenced; this application has matured into a patent. The U.S. Patent Number 6,221,641 must be used as the reference. Correction is required.

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5. The specification is objected to for being confusing as to its conflicting definition of module. On page 6, a module is defined as starting with the N-terminus of a KS domain and ending at the C-terminus of an ACP domain; this, indeed, is the definition found in the art. However, in Example 2, the deletion of sequences upstream of the KS domain of M2 is described to make way for the N-term ERL from M5 of DEBS. Thus, it would seem that M2 contained more than N-term-KS...C-term-ACP. Again in Example 4, the first module of the DEBS PKS cluster “contains the intrapolypeptide linker of the corresponding M1-M2 polypeptide”; while the specification describes the linkers as portions outside the modules. This discussion renders these examples confusing. Clarification is required.

Withdrawn - Claim Objections

6. Previous objection to Claims 28-39 because the word “polyketide” preceding the abbreviation “PKS” is redundant is withdrawn by virtue of Applicant’s amendment.

New – Claim Objections

7. Claim 26 is objected to for having the improper punctuation. Periods after “SEQ” and “ID” are inappropriate.

Withdrawn - Claim Rejections - 35 U.S.C. § 112

8. Previous rejection of Claims 23, 25, 26, and 28-39 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term **intra-molecular linkers (RAL)** is withdrawn. The Examiner has performed an extensive examination of the art to consider how domains, modules, and open reading frames (ORFs) are defined in the PKS art. It appears clear that ORFs are

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simply defined as throughout the art, based on a start and stop codon. Within the ORFs of PKS genes, domains are defined according to structural homologies within the PKS field; these endpoints are quite distinct and are based on functional expression of domains. Modules are simply a collection of domains; thus, modules are also defined according to structural homologies and function expression. The gaps between modules within ORFs, or intrapolypeptide linkers (RALs) as defined by the specification, are clear.

New or Maintained - Claim Rejections - 35 U.S.C. § 112

9. Previous rejection of Claims 23, 25, 26, and 28-39 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term **inter-molecule linkers (ERL)** is maintained, but for different reasons than previously presented. As noted above, ORFs, domains, and modules are clear in the art. There are portions of amino acid sequence at the N-terminus of KS domains (when the KS is in the first module of an ORF) and at the C-terminus of ACP domains (when the ACP is in the last module of an ORF) that are not attributed to the functional KS or ACP domains, respectively. These can be considered N-ERLs and C-ERLs as defined in the specification and are outside the defined modules as clear in the art.

It is unclear, however, whether an N-ERL, a C-ERL or some combination thereof is indicated in the claims. Example 2 in the specification uses the N-ERL from DEBS3 (before M5); Example 5 uses the C-ERL from DEBS1 (after M2). It must be considered that unlike RALs that represent contiguous amino acid sequence, ERLs span coding regions (ORFs) and are not contiguous polypeptide. Moreover, a hybrid PKS polypeptide need not be more than one polypeptide chain. In this case, ERLs are irrelevant.

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The Examiner suggests separation of the RAL and ERL subject matter in the claims to more clearly define what is meant by an ERL and its position in a multi-enzyme (multi-protein) PKS.

10. Previous rejection of Claims 23, 25, 26, and 28-39 under 35 U.S.C. 112, first paragraph, written description, is maintained. Applicants' arguments have been fully considered but are not deemed persuasive. Applicants argue that because the RALs and ERLs are defined in the art, they thus have adequate written description as originally filed. This is not the case. As Applicants point out, "the written description requirement does not necessarily require spelling out sequence of amino acids or nucleotides, provided **the structural features can be ascertained** in a sufficient matter to permit one of ordinary skill in the art to construct them" (emphasis added). It is clear that the structural features *cannot* be ascertained for the RALs or ERLs because they are the *absence* of consensus sequence. They are only defined within the structure of a PKS gene or polypeptide. Without the adjacent KS and/or ACP domains, these RAL and ERL sequences are wholly indiscernible. For these reasons, the Examiner suggests the use of product by process language for the instant claims wherein the RAL and ERL sequences are defined by their adjacent sequences. Such an amendment should obviate the instant rejection.

11. (new) Claims 23, 25, 26, and 28-39 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for hybrid PKSs that effectively result in transfer from a first module to a second module, does not reasonably provide enablement for hybrid PKSs that do not result in effective transfer from a first module to a

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second module. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. To use such hybrid PKSs would require undue experimentation on the art of one of skill in the art.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The instant specification only provides working examples for functioning hybrid PKSs – that is, those which produce some form of polyketide by transferring a nascent polyketide chain from one module to another. It would require copious amounts of unguided experimentation to

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identify other uses of the claimed hybrid PKSs. The state of the prior art is that only functional PKSs are used to produce polyketides; no other functions are evident in the art. It is wholly unpredictability how non-functional hybrid PKS can be used. Thus, the full extent of the scope of the instant claims lacks enablement.

The Examiner notes that the instant rejection was previously presented. The clause that includes “is facilitated” in Claim 23 obviates that previous rejection. However, the Examiner has reconsidered that position. The term “is facilitated” merely requires the assistance to transfer, and does not actually require a functional hybrid PKS. Stronger, positively functional language is required to obviate the instant rejection.

Summary of Pending Issues

12. The following is a summary of the issues pending in the instant application. Each issue must be addressed in a complete response to the instant Office action.

- a) The specification stands objected to for not having updated patent application information.
- b) The specification stands objected to for being confusing as to its conflicting definition of module.
- c) Claim 26 stands objected to for having the improper punctuation.
- d) Claims 23, 25, 26, and 28-39 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the term inter-molecule linkers (ERL).
- e) Claims 23, 25, 26, and 28-39 stand rejected under 35 U.S.C. 112, first paragraph, written description.
- f) Claims 23, 25, 26, and 28-39 stand rejected under 35 U.S.C. § 112, first paragraph, scope of enablement.

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Conclusion

13. Claims 23, 25, 26, and 28-39 are rejected for the reasons noted above. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution. The instant Office action is **NON-FINAL**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



KMK

July 31, 2003